

2011 MEETINGS

The International Symposium on Influenza and Other Respiratory Infections 2011 was held August 2-4, 2011 in Beijing, China. Fabiana Pimenta (DBD/RDB) presented, “Laboratory diagnostics on invasive pneumococcal infections: challenges of existing methods and updates.” Chris Van Beneden (DBD/RDB) presented, “Surveillance for pneumococcal and Hib disease in the United States and Asian countries,” “Antimicrobial use: recommendations from CDC’s Get Smart Program and the global community,” and “Impact of pneumococcal conjugate vaccines in the U.S., before and after universal vaccine introduction.”

On August 8-9, 2011, Fabiana Pimenta (DBD/RDB), Bob Pinner (NCEZID) and Chris Van Beneden (DBD/RDB) conducted a site visit of the International Emerging Infections Program (IEIP) Respiratory Surveillance sites in Jingzhou City, Hubei Province, China.

The National Pertussis Workshop: Strategies to Prevent Severe Pertussis in the Next Decade was held August 25-26, 2011 in Sydney, Australia. Tom Clark (DBD/MVPDB) presented “Vaccine efficacy and vaccine schedules: U.S. overview” and “Cocooning – experience and cost-effectiveness: U.S. overview.”

The XVIII Lancefield International Symposium was held September 4-8, 2011 in Palermo, Italy. Chris Van Beneden (DBD/RDB) presented, “Changing landscape of pneumococcal disease following widespread use of conjugate vaccines in the United States” and the poster, “Does a group A streptococcal strain predict the severity of invasive disease?”

The annual Federation of Infectious Disease Societies of Southern Africa meeting was held September 8-11, 2011 in Durban, South Africa. Stephanie Schrag (DBD/RDB) and Jennifer Verani (DBD/RDB) coauthored a poster, “Invasive group B streptococcal disease in South Africa,” which was presented by an external partner.

The WHO Global New Vaccines Surveillance Meeting was held September 11-14, 2011 in Geneva, Switzerland. Tom Clark (DBD/MVPDB) presented “Lessons learned from Burkina Faso meningitis surveillance strengthening.” Rana Hajjeh (DBD/OD), Stephanie Schwartz (DBD/

(MEETINGS CONTINUED)

OD), Carla Talarico (DBD/RDB), and Chris Van Beneden (DBD/RDB) also actively participated in this meeting.

The 51st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) was held September 17-20, 2011 in Chicago, Illinois. Nancy Messonnier (DBD/MVPDB) presented, “Control of serogroup A meningococcal disease in Sub-Saharan Africa.” Matt Moore (DBD/RDB) presented, “Early impact of 13-valent pneumococcal conjugate vaccine on invasive pneumococcal disease among children <2 years old, U.S, 2010.” Chris Van Beneden (DBD/RDB) presented, “An update on postpartum group A streptococcal infections.”

The 49th Annual Meeting of the Infectious Diseases Society of America (IDSA) was held October 20-23, 2011 in Boston, Massachusetts. Amanda Cohn (DBD/MVPDB) presented, “Meningococcal conjugate vaccine: new recommendations and potential for use of conjugate vaccine in infants.” Lara Misegades (DBD/MVPDB) presented, “DTaP effectiveness: results from the California pertussis vaccine effectiveness assessment.” Sara Tartof (DBD/MVPDB) presented, “Rapid rise of incidence rates of pertussis in the five years following complete DTaP vaccination: is immunity waning earlier than expected?” Andrew Terranella (DBD/MVPDB) presented, “Preventing infant pertussis: a decision analysis comparing prenatal vaccination to cocooning.”

FEATURED PUBLICATIONS

Bradley JS, Byington CL, Shah SS, et al. **The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America.** Clin Infect Dis. 2011;53:e25-76.

CDC. **FDA approval of expanded age indication for a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine.** MMWR. 2011;60(37):1279-80.

CDC. **Legionellosis --- United States, 2000--2009.** MMWR. 2011;60(32):1083-6.

CDC. **Office-related antibiotic prescribing for persons aged ≤14 years --- United States, 1993--1994 to 2007--2008.** MMWR. 2011;60(34):1153-6.

Goldblatt D, Plikaytis BD, Akkoyunlu M, et al. **Establishment of a new human pneumococcal standard reference serum, 007sp.** Clin Vaccine Immunol. 2011;18:1728-36.

Grijalva CG, Moore MR, Griffin MR. **Assessing the effect of pneumococcal conjugate vaccines: what is the value of routinely collected surveillance data?** Lancet Infect Dis. 2011;11:724-6.

Hajjeh, R. **Accelerating introduction of new vaccines: barriers to introduction and lessons learned from the recent *Haemophilus influenzae* type b vaccine experience.** Philos Trans R Soc Lond B Biol Sci. 2011;366:2827-32.

Hicks LA, Chien YW, Taylor TH Jr, et al. **Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996–2003.** Clin Infect Dis. 2011;53:631-9.

Katz LS, Humphrey JC, Conley AB, et al. ***Neisseria* Base: a comparative genomics database for *Neisseria meningitidis*.** Database. Epub ahead of print. Sept 2011.

Lingappa JR, Dumitrescu L, Zimmer SM, et al. **Identifying host genetic risk factors in the context of public health surveillance for invasive pneumococcal disease.** PLoS ONE. 2011;6:e23413.

Marsh JW, Shutt KA, Pajon R, et al. **Diversity of factor H-binding protein in *Neisseria meningitidis* carriage isolates.** Vaccine. Epub ahead of print. Jun 2011

Rudan I, Arifeen SE, Bhutta ZA, et al. **Setting research priorities to reduce global mortality from childhood pneumonia by 2015.** PLoS Med. 2011;8:e1001099.

Tatti KM, Sparks KN, Boney KO, et al. **A novel multi-target real-time PCR assay for the rapid diagnosis of *Bordetella* species in clinical specimens.** J Clin Microbiol. Epub ahead of print. Sept 2011.

Weston EJ, Pondo T, Lewis MM, et al. **The burden of invasive early-onset neonatal sepsis in the United States, 2005–2008.** Pediatr Infect Dis J. Epub ahead of print. Jun 2011.

2011 EPI-AIDS & INVESTIGATIONS

January 27: **Cluster of *Streptococcus pneumoniae* among children living at a psychiatric facility – Rhode Island**

February 18: **Unexplained respiratory disease outbreak associated with conference in Santa Monica, California – Los Angeles, CA**

April 15: **Legionellosis outbreak associated with an acute care hospital – Spokane, WA**

May 21: **Legionnaires’ disease outbreak associated with travel on a cruise ship – New Orleans, LA**

September 3: **Legionnaires’ disease among guests at Resort X, West Virginia – Chester, WV**

September 26: **Legionnaires’ disease among residents of a long term care facility, OH – Columbus, OH**

October 14: **Legionnaires’ disease among travelers to a resort, St. Thomas – Virgin Islands**

regards from
Rana...

I hope you all had a good summer and had the chance to take some time off. The new fiscal year promises to be very exciting for DBD, as we start getting results from many of the studies we began the last few years, embark on new ventures that will increase our understanding of vaccine-preventable diseases and the impact that new vaccines will have in the U.S. and globally.

In the first week of the new fiscal year, as part of QPR, we presented to Dr. Frieden on the TAC assay, an exciting new multi-pathogen respiratory diagnostic platform that is accelerating outbreak control and opening the door for many new investigations in the U.S. and around the world. This highlights yet again the critical role of our laboratories in supporting the division’s work and goals as well as advancing public health. Our critical role is also evident in the many trainings and workshops staff conducted to support the WHO surveillance network that are described in this Bulletin.

We are lucky in our division to have multiple support services for our activities. As you can read about in this Bulletin, we have an excellent statistical unit that is world renowned and has been crucial to our epidemiologic and laboratory activities. Our communications, policy and disease experts staff have contributed significantly to a year-long activity that sought input from the community about meningococcal vaccines as part of a center-wide effort to get more public engagement in vaccines. This activity just concluded with a national stakeholders’ meeting here at CDC.

Though we will be faced with financial and other constraints this fiscal year, I am confident in the ability of our staff to continue to prioritize activities and deliver high quality public health service. I look forward to another fun and productive year!

-Rana

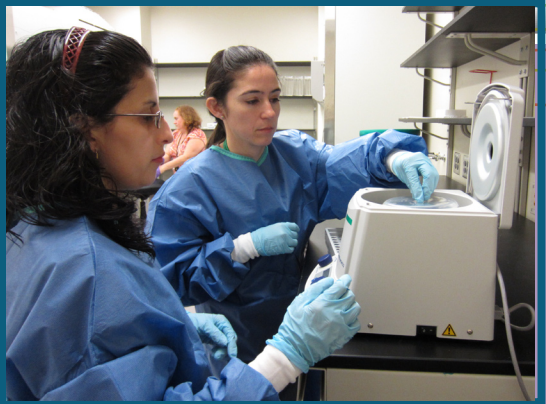


Photo: Maria Renee Lopez (foreground) and Carmen Contreras – from our IEIP partner lab in Guatemala – are preparing a specimen for testing (centrifuging the reagents) while at CDC for training.

TAC: Changing the Way CDC Responds to Outbreaks

The TaqMan® Array Card, known as TAC, (formerly known as the TaqMan® Low Density Array (TLDA) card) is changing the way CDC and the Division of Bacterial Diseases respond to outbreaks. Four Centers at CDC (NCIRD, NCEZID, NCHHSTP, and CGH) are collaborating on optimizing the use of these cards, which became popular after the 2009 H1N1 influenza pandemic.

The premise of TAC is to be able to test for multiple pathogens from a single specimen; at this point, only respiratory specimens have been used. By being able to simultaneously test for multiple pathogens from one specimen, CDC can rapidly identify the etiology of a respiratory outbreak. When the results are suggestive of a certain pathogen, the outbreak specimens are triaged to the appropriate epidemiologists and laboratorians for confirmation testing and to initiate a public health response.

Before TAC was available, each lab at CDC divided a clinical specimen and tested it with their individual wet assays. This testing approach was not only costly (for lab supplies and person time) but also challenging when specimen volumes were minimal, and created a lengthy delay in the turnaround of results. With TAC, the specimen is conserved and testing and response times are significantly shortened. Before TAC, it would take about 20 hours of individual experimental time to analyze 8 clinical specimens for 23 pathogens; with TAC, that time is sliced to approximately 3 hours for similar results.

CDC has been using TAC domestically for the past five years. At this point, laboratorians can look for about 23 pathogens at one time on the card. Jonas Winchell, chief of DBD’s Pneumonia and Response Lab, says, “The huge advantage of TAC is the breadth of organisms you can test for in one specimen.”

With unexplained respiratory disease outbreaks, the card is often called into use unless there is a clear indicator of what pathogen is causing the outbreak.

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TAC has a high rate of success for focusing the investigation and helped guide responses to outbreaks of *C. pneumoniae* in Texas, *M. pneumoniae* in Rhode Island, and adenovirus in Alaska, among others.

Globally, the utility of TAC is being assessed at International Emerging Infections Program (IEIP) field sites along with selected National Influenza Centers (NIC). This is a large pilot study to assess the card’s utility in these settings. TAC is also being used for other international projects, including ones funded by the Bill & Melinda Gates Foundation, like the Aetiology of Neonatal Sepsis in South Asia (ANISA) study.

IEIP and NIC sites recently had an on-site training at CDC’s headquarters in August where 18 people were trained on how to use TAC with the latest instrument that runs these arrays (see photo). The participants enjoyed the hands-on training and commented that, “The combination of theory, experience of the experts, and the practice was the best combination to learn this technique.”

TAC will likely benefit from further evaluation and optimization, especially for field site use. Winchell envisions an eventual technology transfer of the capability to effectively use TAC, possibly to state health departments. This in turn would alleviate some of the laboratory processing burden of CDC, and allow more time to focus on other pressing issues.

Quarterly Program Review (QPR)

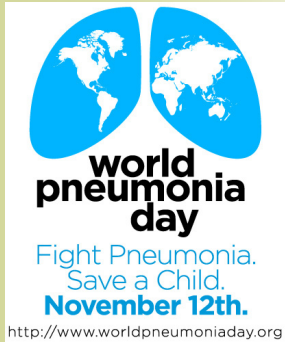
DBD presented an impressive update on division accomplishments since April during the October 5th QPR with Dr. Frieden and his senior staff. In preparation for QPR, the division reviewed and updated its one and four year goals, identifying 21 new goals for the current fiscal year that involve both domestic and global activities. DBD continues to address initiatives in: reducing pneumococcal disease in the U.S.; controlling pneumonia in developing countries; and introducing conjugate meningococcal vaccine in Africa. In collaboration with other programs within NCIRD, the division will lead a new initiative on utilizing the CDC technology for multi-pathogen testing in public health settings (see TAC story).

The Invasive Bacterial Vaccine-Preventable Diseases (IB-VPD) network is a laboratory-based surveillance network started by WHO about two years ago to support introduction of new conjugate vaccines for *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and *Neisseria meningitidis*. The Division of Bacterial Diseases (DBD) serves as the Global Reference Laboratory (GRL) for this network, providing technical support to WHO headquarters and regional offices (AFRO, SEARO, WPRO, PAHO, EMRO and EURO). DBD laboratories have supported WHO regional reference labs (RRLs) in each of these regions to build capacity for detection, isolation and characterization of these organisms and to help them support countries in their regions to conduct surveillance.

Several DBD staff members are involved in GRL activities, with the Respiratory Diseases Branch's *Streptococcus* Laboratory leading the effort, coordinating various training workshops and site visits with the Meningitis Laboratory from the Meningitis and Vaccine Preventable Diseases Branch. In its role as a WHO collaborating center, the Meningitis Lab recently revised and updated the Global Meningitis Laboratory Manual.

Save the Date!

World Pneumonia Day
November 12, 2011
www.worldpneumoniaday.org



Get Smart About Antibiotics Week
November 14-20, 2011
www.cdc.gov/getsmart



The GRL works closely with WHO and other global partners to overcome the challenges involved in improving invasive bacterial disease surveillance by providing ongoing support during training and site visits as well as regular correspondence with the RRLs, and providing assistance with critical supplies and reagents.

Challenges common among developing countries include lack of continuous power supply, inadequate specimen handling and transport conditions and limited supply chains for perishable reagents. Addressing these challenges is critical to strengthening surveillance capacity at the country level to generate the high quality data needed to support countries' decisions for vaccine introduction and to demonstrate vaccine impact post introduction. In addition to providing technical assistance and collaborating with these laboratories, DBD provides epidemiologic expertise for WHO regional offices to enhance the quality of the surveillance data and support better data management, analysis and interpretation.

Recent IB-VPD network activities have included: a site visit and assessment of the Korea CDC Laboratory which serves as RRL for the Western Pacific WHO region; conducting a training workshop for this region in Manila, Philippines in the spring of 2011 (see photo); a joint mission of the GRL and WHO headquarters to the Kenya RRL in Kilifi; sentinel site visits in Uganda; and a specialized training in molecular detection and characterization of agents of IB-VPDs at the Mongolia national laboratory.



Photo: Carla Talarico, from RDB's *Streptococcus* Laboratory, demonstrating isolation and culture techniques of *S. pneumoniae* while working with trainees from the Western Pacific Region during a training course in Manila, Philippines

Ongoing activities include drafting global standard operating procedures in conjunction with WHO; performing quality control/quality assurance for the RRLs as needed; developing training tools such as clinical and laboratory IB-VPD posters for sentinel sites; and updating laboratory manuals.

Consistent with the division's strategic goal of accelerating introduction of new vaccines in countries that need them the most in order to prevent deaths from pneumonia and meningitis and improve child health overall, despite the challenges, DBD remains committed to the IB-VPD network.

The **GAVI Alliance** announced it will provide funding for 16 more developing countries to introduce rotavirus vaccines and 18 more countries to introduce pneumococcal vaccines, noting that the roll out of rotavirus vaccines across Africa has already begun in Sudan. GAVI CEO Seth Berkley, MD said, "Thanks to our donors and partners, the GAVI Alliance is now delivering on its promise to protect more children across the developing world against rotavirus, pneumococcal disease and other life-threatening yet preventable diseases. The death toll of rotavirus and pneumococcal infections in Africa is particularly devastating, and this is where these vaccines will make the most significant impact, not only in lives saved, but also in terms of healthy lives lived. Immunization enables good health and healthy people are more productive and ultimately fuel economic growth." GAVI also approved applications from five countries for pentavalent vaccine, and 12 for other types of vaccines. See detailed list of approved countries at http://www.who.int/immunization/newsroom/press/vaccines_to_reach_37_more_countries/en/index.html

COMMUNICATIONS

A new **scarlet fever** podcast is now available featuring Kathryn Fleming-Dutra discussing scarlet fever, its cause, how to treat it, and how to prevent its spread at <http://www2c.cdc.gov/podcasts/player.asp?f=7458339>.

A new **appropriate antibiotic use** podcast produced by NCIRD, in collaboration with MMWR, has launched. Hear Tarayn Fairlie talk about when acute respiratory infections should be treated with antibiotics and why antibiotics are unnecessarily prescribed at <http://www2c.cdc.gov/podcasts/player.asp?f=8620960>.

On September 20, 2011, Kathleen Dooling, Tarayn Fairlie and Alison Patti, along with staff from the Influenza Division joined ABC News' senior health and medical editor Dr. Rich Besser for a **live Twitter chat** on how to manage illnesses during cold and flu season. Tweets included facts about the common cold, sore throats, and the flu. More than 4.8 million impressions were made, meaning that that many people could have seen a message included in this live chat. Stay tuned for more live chats with Dr. Besser on pneumonia and antibiotic resistance.

Photo: Alison Patti, Kathleen Dooling, and Tarayn Fairlie, along with members of the Influenza Division and CDC's OADC, participate in the Twitter chat.



CDC held four community meetings (organized by contractors, FHI360 and The Keystone Center in collaboration with state and local health departments) this summer to give parents, healthcare providers, health plan administrators and public health officials an opportunity to give their input regarding how to use vaccines that can help protect infants and young children from meningococcal disease. Meningococcal disease is a relatively rare, but often severe illness that can involve swelling of the membranes around the brain as well as loss of limbs from bloodstream infections.

"ACIP and CDC have to consider many things when it comes to determining whether some or all children should be vaccinated against a disease," said senior advisor Glen Nowak, the CDC person overseeing the project. "This includes how well the vaccine works, how much disease can be prevented, how many children are affected, and the costs and benefits associated with vaccination. This project sought to find out how those involved in providing immunizations – doctors, nurses – and members of the public view those factors."

In April, the Food and Drug Administration (FDA) granted a license to Sanofi Pasteur to expand use of its meningococcal conjugate vaccine, Menactra®, to include a two-dose schedule for children 9 months through 23 months of age. This was the first U.S. approval of a meningococcal vaccine for this age group, and two other companies have submitted license applications to FDA. Doctors are permitted to use a vaccine after it has received FDA licensure.

Currently there is no routine recommendation regarding the use of meningococcal conjugate vaccines for healthy children under age 2, but CDC's Advisory Committee on Immunization Practices (ACIP) is likely to soon be evaluating

options for vaccine recommendations for this group.

CDC's National Center for Immunization and Respiratory Diseases held four community meetings in Concorde, NH, Seattle, WA, Chicago, IL, and Denver, CO, this summer to introduce participants to the issues involved in developing immunization recommendations and to seek their views on how best to consider the issues around vaccines that protect children from rare but severe illness. The locations were selected so different parts of the country could be included and because state or local health officials were interested in hosting. DBD's Amanda Cohn, Tom Clark, and Nancy Messonnier each presented scientific information at these meetings.

Prior to the four community meetings, a stakeholder meeting was held in Washington, DC with representatives from around 20 national organizations and interested parties. NCIRD's Anne Schuchat and Glen Nowak, and DBD's Amanda Cohn introduced participants to the public engagement process and provided specific scientific information about meningococcal vaccines and current ACIP recommendations.

This public engagement process had limitations including that the participants in the four community meetings were not necessarily representative of the general public. The meetings did, however, bring together interested people with divergent views and engaged them in a productive dialogue.

A final stakeholder meeting was held October 5th in Atlanta, GA. During this meeting discussions were held to share key findings from the four community meetings, to get input from the stakeholders on the economic and resource factors that should be considered when making immunization policy decisions, and to discuss how methods and approaches like public engagement should be considered in the future to inform ACIP and CDC.

ABCs Multiple Imputation Project

The U.S. Department of Health and Human Services (HHS) recently launched two strategic plans aimed at reducing health disparities. The plans call for HHS to set data standards and upgrade collection and analysis of data on race, ethnicity, primary language and other demographic categories in line with new provisions of the Affordable Care Act. A recent project aimed to improve the quality and usefulness of race reporting as part of the surveillance data generated by the Active Bacterial Core surveillance (ABCs) implemented by Melissa Lewis and Tracy Pondo will help the country track and monitor race-specific and age- by race-specific incidence rates and improve the understanding of racial disparities for disease incidence. The two developed a multiple imputation method as a routine approach for dealing with missing race data, beginning with the 1996 dataset for all ABCs pathogens, and now completed routinely on each new dataset. The two young statisticians are part of the DBD Biostatistics Office which contributes to the planning and execution of analyses across the division and provides innovative statistical approaches to deal with challenging analyses on a daily basis.

Their work was featured at the August 2011 CDC NCHSTP Health Equity Symposium that specifically highlighted the role of data in informing and shaping public health policy, practice, and research and addressing factors of underlying health inequities. The novel approach developed and being used by Lewis and



Pondo, one new to public health surveillance, will keep ABCs and health monitoring activities on par with modern statistical methodology. ABCs is an important active-laboratory-based surveillance system for *Haemophilus influenzae*, *Neisseria meningitidis*, group A *Streptococcus* (GAS), group B *Streptococcus* (GBS) and *Streptococcus pneumoniae* in multiple large diverse U.S. populations. However, race is missing for approximately 15 to 20 percent of reported annual cases. Working with missing data and accurately reflecting uncertainty in the reported incidence rates and risk factor analyses is a challenge. Case reports with missing race information results in a large proportion (15-20%) of ABCs data not being used in standard analysis, and it poses a challenge in correct interpretation of the results.

Lewis and Pondo's multiple imputation method addresses this challenge and will help lead ABCs to better routine race-specific incidence rate reporting, better risk-factor analyses, and analytic consistency among all users of the data in using reported race data. Multiply imputed data provides a dataset with complete data and allows estimation procedures to account for the uncertainty associated with imputing unknown values. This project was only possible with major statistical and methodological enhancements to better improve ABCs.

Photo: Melissa Lewis and Tracy Pondo, from DBD's Biostatistics Office, discussing future uses of multiple imputation with ABCs data.

LCDR Lara Misegades was awarded the USPHS Achievement Medal for "Substantial scientific contributions toward understanding and controlling epidemic meningitis in West Africa as an EIS Officer."

LCDR Lee Hampton was awarded the USPHS Achievement Medal for "Outstanding contributions to improving surveillance for serious pneumococcal disease and for developing national standards for pneumococcal disease reductions in the United States while serving as an EIS Officer."

Keith Klugman, pneumococcal disease expert and regular collaborator with DBD, was honored by the Royal Society of South Africa with the John FW Herschel Medal for contributions to multidisciplinary science in South Africa and in particular for his contribution to the development of conjugate pneumococcal vaccines for Africa and developing countries.

Elizabeth Zell was honored with the 2011 Statistical Science Award honorable mention for demonstrating excellence in science. This was in recognition of the theoretical paper entitled, "Multiple imputation in the anthrax vaccine research program."